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REMARKS

Applicants' attorney is appreciative of the interview granted by the Examiner to the undersigned and to inventor Rene Laversanne on June 13, 2002. At that interview, the inventor explained the difference between the vesicles of the invention and those disclosed in the prior art.

Claims 1-21 have now been canceled, and replaced by new claims 22-41, as follows:

Claims 22-32 are directed to a composition for stabilizing an active agent comprising vesicles of a defined structure containing therein an active agent subject to chemical degradation, and a stabilizer for the active agent;

Claims 33-34 are directed to a method for stabilizing an active agent comprising incorporating the agent and a stabilizer in a liquid crystal lamellar phase, and subjecting the phase to shear to produce vesicles of a defined type;

Claims 35-39 are directed to a composition as in claim 22, but in which the active agent is at least one enzyme;

Claim 40 is directed to a composition as in claim 22, but in which the method for forming the vesicles is recited as in claim 33; and

Claim 41 is directed to a method for increasing the efficacy of a stabilizing agent by method steps as in claim 33. Claim 41 is thought to be supported by the examples of

the present specification in which the efficacy of stabilizing agents is clearly improved.

Claims 1-18 have been rejected under the judicially created doctrine of obviousness-type double patenting over the claims of US Patents Nos. 5,908,697 and 6,277,404.

The claims of the present application require a combination of a vesicle of a defined type, an active agent subject to chemical degradation, and a stabilizer *for the active agent*. The cited references disclose only the vesicles of the defined type and an active agent. There is no disclosure or suggestion of combining the active agent with a stabilizer for the active agent.

The Office Action points out that the claims of the '404 patent recite polymers and polysaccharides, which are disclosed in the present application as stabilizers. However, Applicants consider this recitation to be irrelevant, because the '404 patent *does not recite a combination of these materials with an agent to be stabilized*.

Regarding the surfactant claimed in the '697 patent there is similarly no recitation of a combination of agent and stabilizer for the agent.

Withdrawal of this rejection is requested.

Claim 1-3 and 5 have been rejected under 35 USC 102(b) over CA 2133421.

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The Canadian patent is directed to the preparation of vesicles of the type presently claimed. The Office Action notes that the reference discloses that the vesicles may contain a polymer to structurally stabilize the vesicles.

This disclosure is not what is presently claimed. The present claims require three elements: the vesicles, the encapsulated active agent subject to chemical degradation, and a stabilizer for inhibiting the chemical degradation of the active agent. Stabilization of the structure of the vesicles as disclosed by the reference is unrelated to the purpose of the invention, stabilization of what is in the vesicles.

Withdrawal of this rejection is requested.

Claims 1-8 and 14-16 have been rejected under 35 USC 102(b) over WO 96/31194.

Applicants previously argued that the vesicles of the invention differ from the classical multilamellar vesicles disclosed by the reference, and this argument was rejected in the Final Office action on the basis that in the reference, an aqueous medium is present between the layers, thus alternating with the lipophilic medium.

The vesicles of the invention are defined as including a *regular stack of concentric bi-layers*, a structure which is not present in prior art multilamellar vesicles. Attached hereto is a sheet of photomicrographs, in which the vesicles

can be compared. (Figures 1 and 2 are freeze-fracture, Figure 3 is cryo-TEM.) Figure 1 is a classical multilamellar vesicle in which the bilayers are folded, with a large aqueous core. In Figure 2, in a vesicle of the invention, a concentric series of stacked layers can be seen, with no large aqueous core.

Figure 3 shows a vesicle after dispersion, the regular stacking of layers being maintained.

These photographs give meaning to the terminology, "a regular stack of concentric bi-layers... extending from each vesicle core to periphery, and being separated by an interstitial liquid..." While the prior art vesicles do include alternating layers, they do not possess a regular stack of concentric bi-layers; indeed, it can be seen that the layers do not have a common center, given their folded state.

From comparison of the photographs, it is quite evident that there is a clear structural difference between the vesicles of the invention and those of the prior art, a difference which is defined by the present claims. Withdrawal of this rejection is requested.

Claims 1-8 and 14-19 have been rejected under 35 USC 102(b) over WO 95/18601.

Attached hereto is a full English-language translation of this document in the form of US Patent No. 6,103,259.

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At column 3, lines 3-22, the patent states:

"The process according to the invention makes it possible to incorporate a substance which is active from the pharmaceutical or cosmetic viewpoint, which substance can be incorporated, depending on its nature, either in the aqueous parts or in the parts formed by the surfactants.

Mention may be made, as examples of active substances, of:

dihydroxyacetone (DHA),

alpha-hydroxy acids (fruit acid) and more specifically glycolic, lactic, tartaric and salycilic acids,

water-soluble and liposoluble sunscreening agents, essential oils,

non-saponifiable compounds,

sodium hyaluronate,

micronized TiO_2,

ceramides,

caffeine,

vitamins A, E and C."

In Example 10, the active being encapsulated is salicylic acid. However, there is no teaching that salicylic acid is subject to chemical degradation, or a teaching to also encapsulate a stabilizer for the salicylic acid.

Moreover, vitamins C and E are indeed known to be

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antioxidants, as alleged in the Office Action, but this reference does not teach or suggest associating vitamin C or E with an active that is subject to oxidative degradation. The reference discloses only that vitamins C and E can be encapsulated as actives in the liposomes of the patent.

Since the reference does not teach or suggest the combination of an antioxidant with an active subject to oxidative degradation in a liposome, the reference does not anticipate the claimed invention, and withdrawal of this rejection is requested.

Claims 1-7 and 9-21 have been rejected under 35 USC 102(b) over Munechika et al. It is noted that this is the only rejection applicable to new claims 35-39 (stabilized enzyme compositions).

Initially, it is noted that the liposomes of Munechika et al are classical liposomes and not the multilamellar vesicles of the invention. Reference is made to the figures submitted and discussed with respect to WO 96/31194. For this reason alone, Munechika et al cannot anticipate the claimed invention.

Munechika et al discloses multilamellar liposomes containing lecithin, a surfactant and an drug which can be an enzyme. The vesicles may further contain "stabilizers" as disclosed at col. 3, lines 5-17, such stearylamine,

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cholesterol and polysaccharides. However, these substances are used to *physically* stabilize the structure of the vesicle, and not to prevent *chemical* degradation of an active ingredient enclosed within the liposomes.

There is also a teaching in Munechika et al of the use of an antioxidant to stabilize the lipid (col. 2, line 60) but this also a teaching of stabilizing the lipid structure, not a teaching of adding a stabilizer *for the drug in the vesicles in general, or an enzyme in particular*. Regarding the stability of the incorporated drug, it is disclosed that the method itself (liposome encapsulation) increases the stability of the drug (col. 1, lines 51-56) but there is no teaching of *adding* a stabilizer for the drug incorporated within the liposomes, as is required according to the claimed invention.

Thus, there is no teaching in Munechika et al of the claimed invention, and withdrawal of this rejection is requested.

In view of the foregoing amendments and remarks, Applicants submit that this application is now in condition for allowance. An early allowance of the application with amended claims is earnestly solicited.

Respectfully submitted,

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FIGURE 1

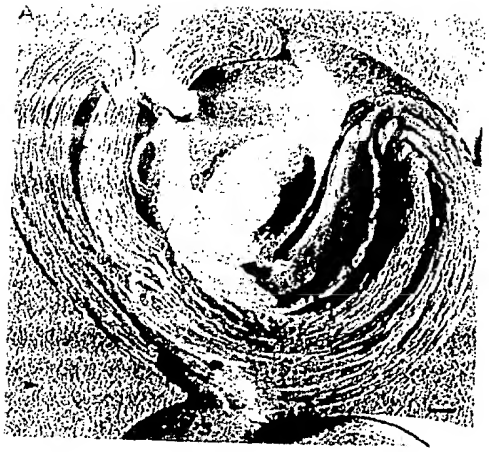

FIGURE 2

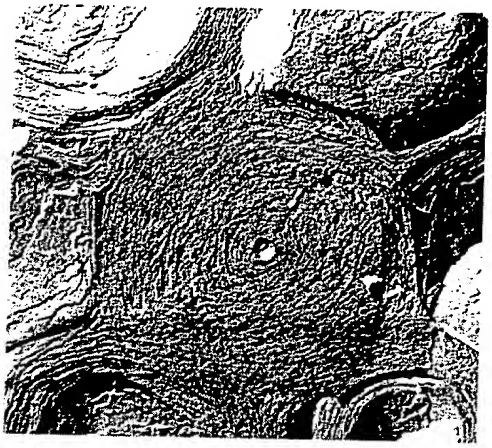

FIGURE 3